

Attorney Docket No.: 6809.230-US  
Filed: January 30, 2004  
Via Facsimile No.: 571-273-8300

Application Serial No.: 10/768,371  
Inventors: Igor Gonda et al.

## IN THE CLAIMS:

1-25 (Cancelled).

26. (Currently Amended) A method of treating diabetes mellitus in a diabetic patient in need thereof, by reproducibly dosing insulin for systemic effect to the patient's circulatory system via the patient's lungs in order to obtain an acceptable blood glucose level in the diabetic patient thereby reducing or eliminating the need for injection of insulin in the diabetic patient wherein the patient lacks the ability to maintain an acceptable blood glucose level without medical treatment, said method comprising:

(a) supplying a predetermined amount of powdered insulin to a hand held device, said predetermined amount being in excess of that amount required, in the bloodstream of said patient, to produce or maintain an acceptable serum glucose level in said patient;

(b) exhaling;

(c) contacting said insulin with a compressed gas to form a cloud in said hand held device, said cloud comprising a repeatable amount of insulin, said repeatable amount being in excess of that amount required, in the bloodstream of said patient, to produce or maintain an acceptable serum glucose level in said patient, said cloud comprising insulin particles in the range between 0.25 and 6 microns; and

(d) inhaling said cloud at an inspiratory flow rate in the range of 0.1 to 2.0 liters per second and wherein the inhaling of said cloud occurs with a high volume that comprises total inhaled volume of 65% to 100% of the patient's lung total lung volume capacity;

(e) producing an acceptable blood glucose level in the diabetic patient ~~who in the absence of steps a-d would not have an acceptable blood glucose level~~, wherein the acceptable blood glucose level is produced by systemically absorbing a controlled dose of insulin that comprises a percentage of the supplied amount of powdered insulin.

27. (Previously Presented) The method of claim 26, wherein the inhalation in the inhaling step is performed by making a maximal effort to inhale.

28. (Currently Amended) The method of claim 26, wherein the aerosolization occurs with a

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compressed gas, having a aerosol is comprised of human insulin particles between about 1 and 4 microns and occurs with a pressure less than 400 psi.

29. (Currently Amended) The method of claim 26 wherein the patient is a patient with type II diabetes, and wherein the insulin cloud comprises human insulin particles having a size in the range of about 1-3 microns.

30. (Previously Presented) The method of claim 26, further comprising repeating steps a-c, wherein in each repetition of steps a-e, the patient inhales substantially the same volume of air with the cloud of insulin.

31. (Previously Presented) The method of claim 30, wherein the inhaling occurs at substantially the same flow rate.

32. (Currently Amended) A method of treating diabetes mellitus in a patient in need thereof, by administering insulin replacement therapy for systemic effect delivered by inhalation in order to eliminate or reduce the need for injections of insulin wherein the patient lacks the ability to maintain an acceptable blood glucose level without medical treatment, said method comprising:

supplying a predetermined amount of powdered insulin to a mechanical hand held device, said predetermined amount being in excess of that amount required, in the bloodstream of said patient, to produce or maintain an acceptable serum glucose level in said patient;

contacting said insulin with a compressed gas to form a cloud in a given area of said hand held device, said cloud comprising a repeatable amount of insulin, said repeatable amount being in excess of that amount required, in the bloodstream of said patient, to produce or maintain an acceptable serum glucose level in said patient, said cloud comprising insulin particles in the range between 0.5 and 6 microns 0.25 and 6 microns;

exhaling a determined volume of air;

inhaling said cloud at an inspiratory flow rate in the range of 0.1 to 2.0 liters per second and wherein the inhaling of said cloud occurs with a high volume that comprises total inhaled volume of 65% to 100% of the patient's lung total lung volume capacity;

producing an acceptable blood glucose level in the a patient who in the absence of steps would not have an acceptable blood glucose level, wherein the acceptable glucose level is

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produced by systemically absorbing a controlled dose of insulin that comprises a percentage of the supplied amount of powdered insulin;

repeating the above steps when the patient's blood glucose levels rise or are expected to rise above a predetermined range and wherein for each repetition of the inhalation, the patient inhales substantially the same total volume.

33. (Previously Presented) The method of claim 32, wherein the insulin cloud is administered to the patient at substantially the same point of inspiration each time the inhaling step is repeated and wherein the patient continues to inhale after the cloud is inhaled and wherein the inhalation continues to a determined point in the inspiratory cycle that is substantially the same each time the inhaling step is repeated.

34. (Currently Amended) A method of administering a controlled and repeatable dose of insulin to a diabetic patient that is sufficient to control the patient's blood glucose level, the method comprising the steps of:

supplying a predetermined amount of dry insulin powder to a hand held mechanical inhalation device;  
contacting the powder with a volume of air in a given area of the hand held device to form a standing cloud comprised of human of insulin particles and air in the given area of the hand held device;

exhaling a volume of air;

inhaling the insulin and air cloud, followed by continual inhalation with additional air until a determined point of inspiration is reached, wherein the point is a point  $V_{(h)}$  corresponding to a high volume and wherein it is determined by coaching (by teaching) the patient to inhale to high volume, which corresponds to 65% to 100% of total lung volume;

wherein when the above steps are repeated in order to administer subsequent doses of insulin the patient, as a result of the coaching, inhales each subsequent dose with about the same high volume by inhaling to about the same determined point  $V_{(h)}$ , substantially the same total volume is inhaled during each repetition of the inhaling step by inhaling to substantially the same determined point during each repetition

35. (Previously Presented) The method of claim 34, wherein the determined point is determined by making a maximal effort to inhale.

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36. (Previously Presented) The method of claim 34, wherein the exhaled volume is a determined volume and when the steps are repeated in order to administer subsequent doses each determined volume of exhaled air is substantially the same.
37. (Currently Amended) The method of claim 36 34, wherein the flow rate during inhalation is maintained at a rate of under 2 liters per second, and wherein the inhaling step is immediately followed by a breath holding step that comprises performing a breath hold for a predetermined period of time.
38. (Previously Presented) The method of claim 37, wherein the flow rate during inhalation is substantially the same for each repetition of the inhalation.
39. (Currently Amended) The method of claim 36 37, wherein the insulin cloud is inhaled before the patient inhales 0.8 liters of air.
40. (Previously Presented) The method of claim 39, wherein the total inhaled volume during the inhalation step is a determined volume that is determined by coaching the patient to perform a specific breathing maneuver.
41. (Previously Presented) The method of claim 40, wherein the specific maneuver comprises inhaling with a maximal effort.
42. (Currently Amended) The method of claim 39 41, wherein the inhaling occurs at a flow rate ~~between 0.5 and 1~~ under about 1 liters per second and wherein the flow rate for each repetition of the inhaling step is substantially the same.
43. (Previously Presented) The method of claim 42, wherein the inhaling of the insulin cloud occurs at substantially the same accumulated inspiratory volume for each repetition of the inhaling step, and wherein the method further comprises a breath holding step immediately after the inhaling step and wherein for each repetition the breath holding step comprises holding of breath for substantially the same predetermined period of time.
44. (Currently Amended) The method of claim 43, wherein the determined point in each repetition of the inhaling step results in a determined volume being inhaled wherein the determined volume is substantially the same for each inhaling step and wherein the determined volume is determined by coaching a patient to perform a specified breathing

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maneuver, wherein the insulin cloud comprises a mixture of insulin and air having a volume of 200-400 ml and wherein the specific breathing maneuver comprises inhaling the 200-400 ml of air entrained with insulin followed by inhaling maximally to 65 to 100 % of lung capacity.

45. (Previously Presented) The method of claim 26, further comprising the step of performing a breath hold for a predetermined period of time immediately after the inhaling step.
46. (Previously Presented) The method of claim 32, further comprising the step of performing a breath hold for a predetermined period of time immediately after the inhaling step.
47. (Previously Presented) The method of claim 34, further comprising the step of performing a breath hold for a predetermined period of time immediately after the inhaling step.
48. (Cancelled)
49. (Currently Amended) The method of claim 26 48, wherein the insulin is human monomeric insulin.
50. (Currently Amended) The method of claim 32, wherein the insulin is human ~~an~~ insulin analog.